Established 1773
11, CHANDOS ST. CAVENDISH SQ.

A CONTRIBUTION TO THE STUDY OF

PHLYCTENULAR OPHTHALMIA

BY

J. B. NIAS, M.D. Oxon., M.R.C.P. Lond.
PHYSICIAN TO THE WESTERN GENERAL DISPENSARY, MARYLEBONE-ROAD, N.W.;
AND
LESLIE PATON, M.B. Cantab., F.R.C.S. Eng.
OPHTHALMIC SURGEON TO ST. MARY'S HOSPITAL, PADDINGTON, W.

(From the Pathological Laboratory of St. Mary's Hospital.)

Reprinted from THE LANCET, December 1, 1906.

Established
1773
384

Established 1773
11, CHANDOS ST. CAVENDISH

A CONTRIBUTION TO THE STUDY OF PHLYCTENULAR OPHTHALMIA.

THE idea that phlyctenular ophthalmia is due to infarctions of dead or attenuated tubercle bacilli has occurred to many clinical observers. It is a hypothesis that suits very well the recognised features of the disease, but no direct verification has hitherto been obtained in support of it either from the histological or from the experimental side. By a recent employment, however, of the delicate methods invented by Sir A. E. Wright and his collaborators for measuring the fluctuations that are produced in the opsonic power of the blood by the invasion of pathogenic organisms, we believe that we are able to throw some light upon this vexed question.

During the past 12 months, acting upon a suggestion of Sir A. E. Wright, we have been testing the opsonic power of the blood against the tubercle bacillus in all cases of phlyctenular conjunctivitis that have presented themselves in the out-patient department of St. Mary's Hospital. The number so examined is now well over 50 and the samples of blood examined amount to nearly 200, so that we may claim to have established a broad basis for our conclusions. A preliminary note on the results was presented to the Ophthalmological Society in November, 1905,[1] in which, without putting forward any very positive conclusion, we were able to announce that the blood of such patients behaved in a manner which was altogether typical of a definite tuberculous infection—that is to say, that its activity in opsonic action on the tubercle bacillus fluctuated in a marked and definite manner above and below the normal according to the progress of the case. Since that time we have proceeded in a more elaborate fashion by procuring the attendance of patients at the laboratory for the daily sampling of their blood, and it is a selection from the much more conclusive data so obtained that we wish to submit on the present occasion.

---

[1] Transactions of the Ophthalmological Society of London, vol. xxvi., p. 232.

The blood of a patient suffering from genuine phlyctenular ophthalmia is generally found to be markedly deficient in opsonic power to the tubercle bacillus but not to other bacteria, such as the staphylococcus, at the outset of the case, but if the patient be adequately treated (without recourse to tuberculin, be it understood) the opsonic index rapidly rises and reaches a maximum coincidently with the healing of the ulcers. It then begins to fall rapidly and in a few days is far below the normal, as if from exhaustion of the mechanism. At this low figure it will remain if the observations be continued for an indefinite time, and if, as so often occurs, a relapse takes place the same sequence of phenomena will be reproduced. In a minority of cases, generally older and more vigorous subjects, the opsonic index as regards tubercle will be found to have risen already much above the normal. Here it will remain with temporary falls till healing occurs and then takes a terminal drop as in the former category. We have not yet met with a single exception to this course of phenomena in phlyctenular conjunctivitis.

The simplest type of case is presented in Chart 1. The patient, a girl, aged 18 months, was a badly nourished child who was taken to St. Mary's Hospital for a well-marked ulcer on the margin of the cornea on August 18th, 1905, with the usual photophobia and blepharo-spasm. Treatment was initiated with iodide of iron, atropine ointment, and fomentations, and the patient continued in attendance until Oct. 31st, when she was discharged cured. The blood was only examined for its opsonic index on one occasion during this attack—namely, on Sept. 1st, and the index was found to be 1·0—i.e., normal. On Jan. 25th of the present year she was brought back with a fresh attack and this time it was determined to have a complete record of the case. Accordingly the mother was persuaded to bring the child as nearly as possible daily to the laboratory and the annexed chart was obtained. The eye presented a single phlyctenular ulcer on the edge of the right cornea; yellow oxide of mercury ointment was used on this occasion with a mixture of rhubarb and soda internally, the child's digestion being disordered. In a week's time the ulcer had healed and the chart shows that during that time the opsonic index had steadily risen from 0·5 to 0·95. It continued to rise to 1·5 and fell to 1·2. The child was then transferred to the medical department and attended there until the 23rd, when she was discharged. We have not seen her since.

CHART 1.

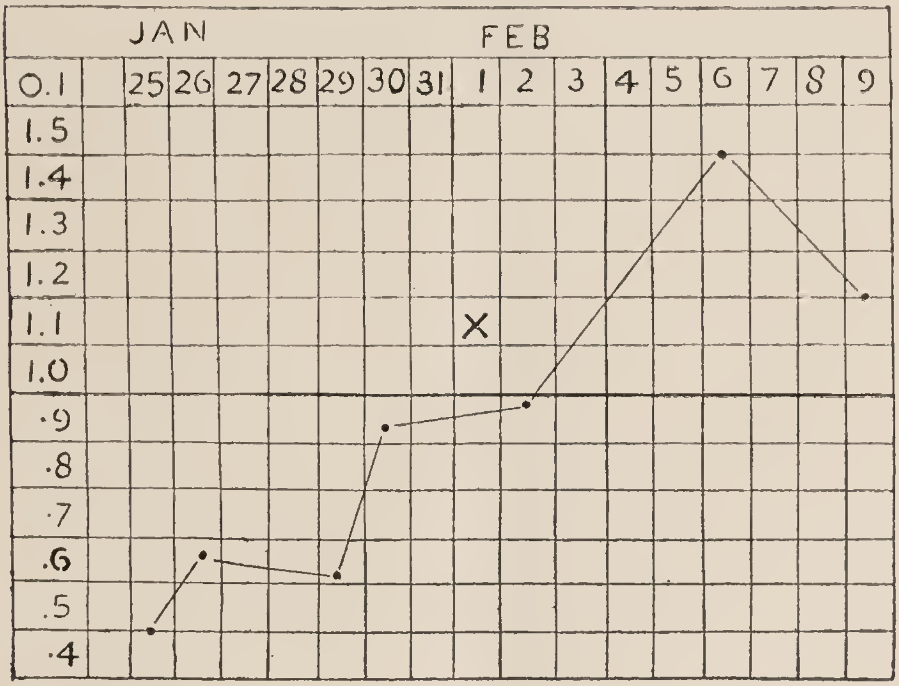

Chart of opsonic index. X, Disappearance of ulcer.

No very palpable tuberculous lesion could be detected in this child, though the usual surmises may be made as to the existence of enlarged mesenteric glands and so forth. In the present state, however, of our knowledge as to the effect on the blood of declared tuberculous disease it is difficult to believe that such a chart could be derived from a patient without a slumbering focus of tuberculous disease somewhere in the body. The great majority of cases of phlyctenular ophthalmia yield charts of this type.

Chart 2 is a less pronounced instance of the same class. The patient, aged 10 years, was a healthy-looking boy who came to St. Mary's Hospital on Jan. 9th of the present year with two marginal ulcers on the right cornea and three on the left. His clinical history was good, but he had undoubtedly had two attacks of the same affection before. Treatment was begun with yellow oxide ointment, fomentations, and iodide of iron. By attendance at the laboratory a very satisfactory chart (Chart 2) was obtained; the opsonic index was found to hover around the normal for several days and then rose to 1·4, to be followed by the usual terminal drop to 0·67. The ulcers began to improve after four days' treatment and were gone in a week. On August 3rd this boy returned to the hospital with a doubtful kind of conjunctivitis on the outer side of the left eye said to have followed a blow. Arrangements were made to obtain a fresh chart, but had to be abandoned from press of other work. Three samples of blood were, however, tested as follows: August 3rd, 0·47; August 4th, 0·74; August 6th, 1·20; therefore, this was probably the development of another ulcer which would have followed the usual course

CHART 2.

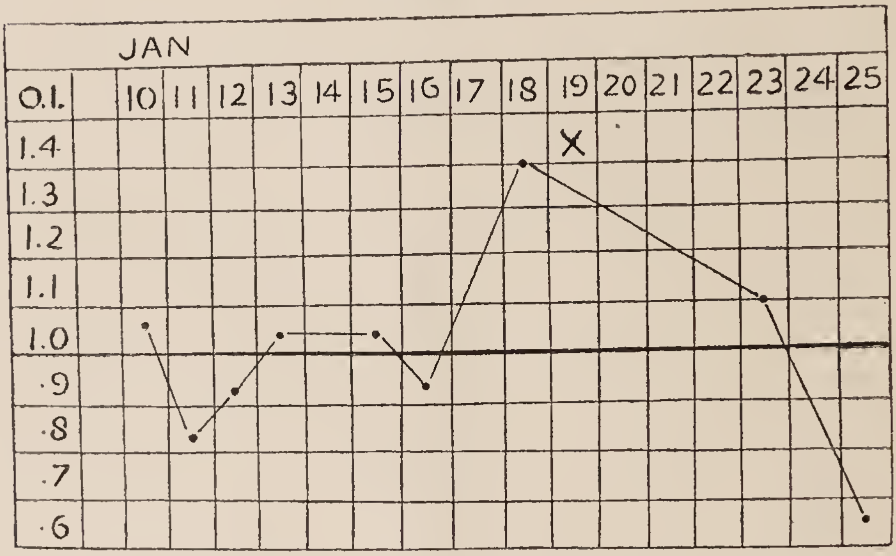

Chart of opsonic index. X, Disappearance of ulcer.

A condition which occurs in 8 or 10 per cent. of the cases is shown in Charts 3 and 4. Here the patient's blood is found to be far above the normal in its opsonic power towards the tubercle bacillus, presumably from having risen before the patient comes under observation. It is generally older and more vigorous patients who show this prompt reaction. Chart 3 is that of a girl, aged 14 years, who had just recovered from an attack of chicken-pox. She presented two typical ulcers on the right eye and one on the left. A history was given of a former attack a year previously and some enlarged glands could now be felt in her neck. Treatment consisted of a mixed ointment of yellow oxide and atropine fomentations and iodide of iron. Through the goodwill of the patient an excellent chart was procured ; and in view of the anomalous figures obtained great pains were taken with the estimation of the blood, which we believe to be quite correct and free from errors of technique. If there be any value whatever in the method of research elaborated by Sir A. E. Wright and his co-workers this is a surprising

CHART 3.

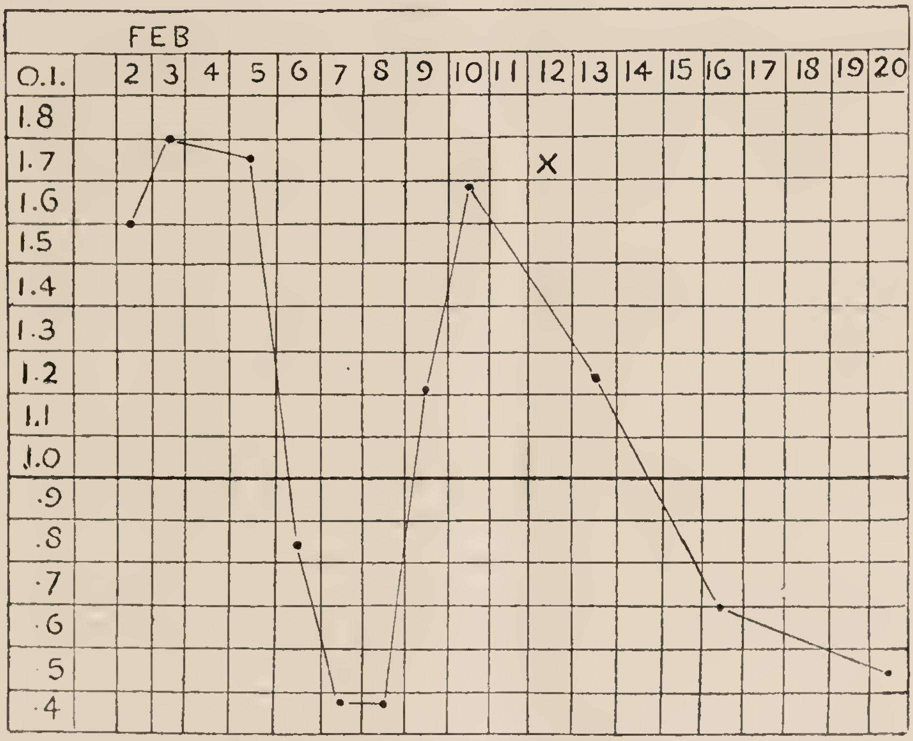

Chart of opsonic index. X, Disappearance of ulcer.

example of the results which it yields. Clinically there was nothing remarkable about the aspect of the case and yet the blood was undergoing these marked variations in its composition or activity. It will be seen that at first the opsonic index ranged from 1·6 to 1·8; then from what we are tempted to consider an over-production of the protective substance, what Sir A. E. Wright has denominated a "negative phase," ensued; and the opsonic index fell on two successive days to 0·47. So surprising was this that the samples of blood were worked twice over. A final rise took place to 1·7 and the ulcers healed. Feb. 10th was a Saturday and the estimation of the blood was finished before the patient's arrival on Monday; from the figure of the opsonic index it was predicted that the ulcers would be quite healed, as

Chart 4.

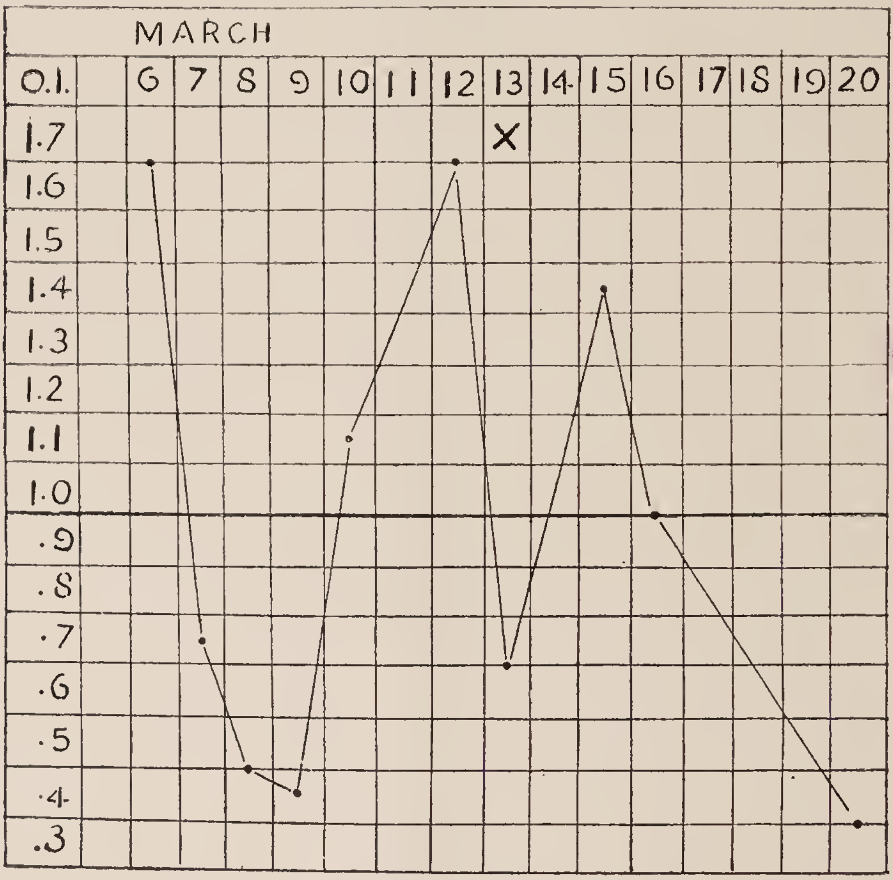

Chart of opsonic index. X, Disappearance of ulcer.

was the case. On the strength of our experience we can now foretell either the speedy healing of an unpromising looking case or the probable delay in the final cure of a comparatively trivial one. Never in our experience do phlyctenules get well without this rise in the opsonic power.

There is not room on the chart to display an interesting relapse which this girl had. From Feb. 20th her index continued to fall until on the 25th it descended to 0·30—that is, practically, her serum had no opsonic power on the tubercle bacillus. On the 27th she developed a fresh phlyctenule in the left eye; on March 6th the index had risen again to 1·75, and on the 7th this ulcer too disappeared. The patient now developed a gumboil and boils in the axilla and was ill for a week. This did not affect in the least the index to tubercle which was again 1·75 on the 13th; from this point it declined until at her weekly visit on the 20th it was 0·45. From this it rose again to 0·85, when her attendance at the hospital finally terminated, she being then in good health To those who have not followed the researches of Sir A. E. Wright and his school upon the subject of the opsonic power of the blood these figures may seem unmeaning; but to others they are full of significance and it is difficult to escape from the conclusion that in this patient we were studying the vagaries of a genuine tuberculous infection.

Chart 4 is that of another girl, aged 16 years, from whom we were able to obtain a very complete record. The clinical notes of the case are missing, but it needs no comment. It is introduced principally to show a second instance of the sudden intermediate drop which we have ascribed to overproduction of defensive substance; in this case there was no relapse.

The foregoing are typical examples of the results which we have obtained from a long series of carefully investigated cases of this affection, treated without having recourse to tuberculin, which would, of course, vitiate the results. Several times we have been tempted to have recourse to this agent but have always found the established methods of treatment equal to the occasion if carefully and assiduously applied. We may therefore characterise the cases as on the whole left to themselves.

Before entering on any elaborate discussion of the phenomena we have described, our first desire, of course, is to have them verified or contradicted by other observers, to whom, however, we would suggest one caution—namely, not to be satisfied with mere casual estimations of the opsonic index in this or that case but to follow it through to the end and face the labour and trouble involved, which may be considerable. All we shall say now is that our observations in the present state of our knowledge go far to furnish support for the hypothesis of Leber and other eminent authorities that these ulcers are due to attenuated or dead bacilli escaped from some unidentified focus of tuberculous disease, either free or taken up by leucocytes and not having sufficient vitality to generate a typical tuberculous lesion at their new site.

The starting point of this investigation was the occurrence of a certain number of cases of undoubted phlyctenular ophthalmia among patients who were attending the pathological laboratory of St. Mary's Hospital for treatment of various tuberculous affections by regulated doses of tuberculin. It appeared to Sir A. E. Wright that the coincidence was more than accidental and he invited us to examine the subject systematically with the result set forth. For much sympathetic advice and assistance we have to tender him our best thanks, as also for the unlimited use of the facilities of his laboratory.

Printed at The Lancet Office, 423, Strand, W.C.